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APR 14 2008

## Amendment and Response

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Serial No.: 10/780,797

Confirmation No.: 1508

Filed: February 17, 2004

For: USE OF INHIBITORS OF INDOLEAMINE-2,3-DIOXYGENASE IN COMBINATION WITH OTHER  
THERAPEUTIC MODALITIESAmendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. (Previously Presented) A method of treating a subject with a cancer, the method comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, and administering at least one additional therapeutic agent, wherein the administration of the inhibitor of indoleamine-2,3-dioxygenase and the at least one additional therapeutic agent demonstrate therapeutic synergy, wherein the at least one additional therapeutic agent is a cytotoxic antineoplastic chemotherapy agent, and wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of 1-methyl-tryptophan,  $\beta$ -(3-benzofuranyl)-alanine,  $\beta$ -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan.
2. (Original) The method of claim 1, wherein the indoleamine-2,3-dioxygenase-mediated immunosuppression is mediated by an antigen presenting cell (APC).
3. (Canceled)
4. (Previously Presented) The method of claim 1, wherein the antineoplastic chemotherapeutic agent is select from the group consisting of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, vincristine, ifosfamide, cisplatin, gemcitabine, busulfan, ara-C, and combinations thereof.
5. (Withdrawn) A method of treating a subject with a cancer, the method comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, and administering at least

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one additional therapeutic agent, wherein the administration of the inhibitor of indoleamine-2,3-dioxygenase and the at least one additional therapeutic agent demonstrate therapeutic synergy, wherein at least one additional therapeutic agent is radiation therapy, and wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of 1-methyl-tryptophan,  $\beta$ -(3-benzofuranyl)-alanine,  $\beta$ -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan.

6. (Withdrawn) The method of claim 5 wherein the radiation therapy is localized radiation therapy delivered to the tumor.

7. (Withdrawn) The method of claim 5 wherein the radiation therapy is total body irradiation.

8. (Cancel)

9. (Original) The method of claim 1 wherein the inhibitor of indoleamine-2,3-dioxygenase is 1-methyl-tryptophan.

10. (Withdrawn) The method of claim 5 wherein the inhibitor of indoleamine-2,3-dioxygenase is 1-methyl-tryptophan.

11. (Previously Presented) The method of claim 1 wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of the D isomer of 1-methyl-tryptophan, the D isomer of  $\beta$ -(3-benzofuranyl)-alanine, the D isomer of  $\beta$ -(3-benzo(b)thienyl)-alanine, and the D isomer of 6-nitro-D-tryptophan.

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12. (Withdrawn) The method of claim 5 wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of the D isomer of 1-methyl-tryptophan, the D isomer of  $\beta$ -(3-benzofuranyl)-alanine, the D isomer of  $\beta$ -(3-benzo(b)thienyl)-alanine, and the D isomer of 6-nitro-D-tryptophan.

13. (Original) The method of claim 1, wherein the cancer is selected from the group consisting of melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer, and Kaposi's sarcoma.

14-29. (Cancel)

30. (Previously Presented) The method of claim 1 further comprising administering a cytokine.

31. (Original) The method of claim 30 wherein the cytokine is granulocyte-macrophage colony stimulating factor (GM-CSF) or flt3-ligand.

32. (Previously Presented) A method of augmenting the rejection of tumor cells in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan,  $\beta$ -(3-benzofuranyl)-alanine,  $\beta$ -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the rejection of tumor cells obtained by administering both the inhibitor of indoleamine-2,3-dioxygenase and the cytotoxic antineoplastic chemotherapeutic agent is greater than that obtained by administering either the inhibitor of indoleamine-2,3-dioxygenase or the cytotoxic antineoplastic chemotherapeutic agent alone.

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33. (Previously Presented) A method of treating cancer, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan,  $\beta$ -(3-benzofuranyl)-alanine,  $\beta$ -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the cancer survival rate observed by administering both the inhibitor of indoleamine-2,3-dioxygenase and the cytotoxic antineoplastic chemotherapeutic agent is greater than the cancer survival rate observed by administering either the inhibitor of indoleamine-2,3-dioxygenase or the cytotoxic antineoplastic chemotherapeutic agent alone.

34. (Previously Presented) A method of reducing tumor size or slowing tumor growth in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan,  $\beta$ -(3-benzofuranyl)-alanine,  $\beta$ -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one cytotoxic antineoplastic chemotherapeutic agent, wherein the tumor size or tumor growth observed with the administration of both the inhibitor of indoleamine-2,3-dioxygenase and the cytotoxic antineoplastic chemotherapeutic agent is less than the tumor size or tumor growth observed with the administration of either the inhibitor of indoleamine-2,3-dioxygenase or the cytotoxic antineoplastic chemotherapeutic agent alone.

35. (Withdrawn) A method augmenting rejection of tumor cells in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan,  $\beta$ -(3-benzofuranyl)-alanine,  $\beta$ -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy, wherein the rejection of tumor cells wherein the rejection of tumor cells obtained by administering both the inhibitor of indoleamine-2,3-dioxygenase and the radiation therapy is greater than that obtained by administering either the inhibitor of indoleamine-2,3-dioxygenase or the radiation therapy alone.

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36. (Withdrawn) A method of treating cancer, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan,  $\beta$ -(3-benzofuranyl)-alanine,  $\beta$ -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy, wherein the cancer survival rate observed by administering both the inhibitor of indoleamine-2,3-dioxygenase and radiation therapy is greater than the cancer survival rate observed by administering either the inhibitor of indoleamine-2,3-dioxygenase or radiation therapy alone.

37. (Withdrawn) A method of reducing tumor size or tumor growth in a subject, the method comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan,  $\beta$ -(3-benzofuranyl)-alanine,  $\beta$ -(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy, wherein the tumor size or tumor growth observed with the administration of both the inhibitor of indoleamine-2,3-dioxygenase and radiation therapy is less than the tumor size or tumor growth observed with the administration of either the inhibitor of indoleamine-2,3-dioxygenase or radiation therapy alone.

38. (Withdrawn) The method of claim 5, wherein the indoleamine-2,3-dioxygenase-mediated immunosuppression is mediated by an antigen presenting cell (APC).

39. (Withdrawn) The method of claim 5, wherein the cancer is selected from the group consisting of melanoma, colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, leukemia, brain tumors, lymphoma, sarcoma, ovarian cancer, and Kaposi's sarcoma.